



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

ATTY.'S DOCKET: VESPER=1

In re Application of:)	Art Unit: 1645
)	
Stephen J. VESPER)	Examiner: Patricia A. DUFFY
)	
Appeal No.: 2006-3008)	Confirmation No. 5682
)	
Appln. No.: 09/866,793)	
)	
Filed: May 30, 2001)	Washington D.C.
)	
For: METHODS FOR ISOLATING)	February 22, 2007
AND USING FUNGAL...)	

SECOND SUPPLEMENTAL REPLY BRIEF

Honorable Commissioner for Patents
U.S. Patent and Trademark Office
Customer Service Window, Mail Stop Appeal Brief-Patents
Randolph Building
401 Dulany Street
Alexandria, VA 22314

Sir:

Supplemental to the Supplemental Reply Brief of
January 17, 2007, please enter the following Second
Supplemental Reply Brief:

STATUS OF THE CLAIMS

Claims 1-22 have been cancelled. Claims 34-38 have
been withdrawn. Claims 23-33 stand rejected.

SUMMARY OF CLAIMED SUBJECT MATTER

The present invention is directed to methods for detecting exposures to fungi in a species-specific manner. This invention is based on the discovery that fungi that were previously not known to produce hemolysins do indeed produce these proteins, which are species-specific. This is useful because different fungi are associated with different diseases. The knowledge of the specific fungus causing the disease can affect prevention methods or treatment protocols. Therefore, it is critical to be able to differentiate human or other animal exposures to a specific fungus, so that the proper medication at the proper dosage can be administered in a timely fashion.

The present invention provides that these same specific hemolysins can be used to quantify the specific fungi in environmental samples. This is useful because one could monitor a hospital, workplace, or home for the presence of problematic fungi in a timely fashion, possibly preventing exposures of the people or animals in these environments.

Although it has been known for years that certain fungal pathogens such as *Candida albicans* and *Aspergillus fumigatus* produced hemolysins, the present invention describes for the first time that other fungi also produce hemolysin. The present application teaches how to use this knowledge to

provide a useful product/service for the medical and environmental communities. That is, using the process of the present invention, one can determine which if any fungi are present in a sample.

The fungal hemolysin protein may be present in blood, serum, urine, saliva or other measurable body fluid of a human or other animals exposed to the fungus. If the fungus is present in the environment, such as a building, a sample from, e.g., a wall or floor of the building can be taken to determine if a fungus is present in the building or other environment. The method of measurement is not critical and can include GC-MS, MALDI-tof, immunoassays such as ELISA and RIA, or the like.

Claim 23 is directed to a method for determining if an animal has been exposed to a specific hemolysin-producing fungus, which hemolysin is species-specific, by contacting a sample from an animal with labeled antibodies that bind only to the hemolysin produced by the fungus, detecting any complex formed, and correlating presence of a complex with exposure to a fungus (specification, paragraphs 0012, 0021, 0032, 0033).

Claim 27 is directed to a method for determining if an animal has been exposed to a specific hemolysin-producing fungus as above wherein the fungal hemolysin used to prepare the labeled antibodies is isolated by culturing a strain of

fungus and isolating hemolytically active fractions of fungal hemolysin (specification, paragraphs 0014, 0025-0033).

Claim 30 is drawn to a method for determining if a building containing hemolysin-producing fungi by assaying a sample from a building in a manner similar to assaying a sample from an animal (specification, paragraphs 0018, 0024, 0036, 0037).

Claim 33 is directed to a method for determining if an animal has been exposed to a specific hemolysin-producing fungus by detecting the presence of the hemolysin produced by the fungus in a sample from the animal, the presence of the hemolysin in the sample indicating that the animal has been exposed to the specific hemolysin-producing fungus (specification, paragraphs 0012, 0021, 0032, 0033).

Claim 35 is directed to a method for determining if a building contains fungi which may be deleterious to occupants of the building comprising obtaining a strain of fungus from the building, culturing the fungus, applying the culture filtrate to a plate, and detecting the presence of hemolysin in the plate (specification, paragraphs 0024, 0036, 0037).

I. Claims 23 and 25-29 are not Unpatentable under 35 U.S.C. 103(a) over Sakaguchi et al. in view of Harlow

It is respectfully submitted that the entire application is based upon the premise that hemolysin producing fungi produce hemolysins that are specific to each fungus. It is clear from paragraph 0024 of the specification as filed that the hemolysins produced by the fungi are specific to each fungus. Otherwise, an assay for an individual fungus would be impossible. Paragraph 0034 states:

Exposure to low levels of hemolysin can lead to potassium ion depletion in monocytes, which can lead to activation of interleukin-converting enzyme. This in turn can lead to rapid and massive release of mature IL-beta. In addition, T-lymphocytes that leak potassium ions undergo programmed cell death (apoptosis). For this reason, it is critical to identify the source of the hemolysin in a human or other animal which may have been exposed to a hemolysin-producing fungus and immediately begin treatment. [emphasis added]

It is clear from the above that hemolysins specific to each fungus are needed in order to identify the source of the hemolysin. That is, one must identify the fungus that produced the hemolysin so that treatment can begin.

It is respectfully submitted that the Examiner has misquoted paragraph 0024 of the specification as filed. This paragraph reads, "By growing strains of hemolysin producing fungi *in vitro* and isolating the hemolysin it is now possible to use the protein obtained to identify fungi which are

isolated from buildings, homes, schools and the like."

[emphasis added]

There is nothing in Sakaguchi that even suggests that individual hemolysins can be used to identify individual fungi. Sakaguchi knew that the rat had been exposed to the fungus, and was trying to determine how the infection progressed through the rat's tissues. The methods claimed herein, however, are for determining if an animal has been exposed to a specific hemolysin-producing fungus. Since Sakaguchi already knew that the rat had been exposed to the fungus, the Sakaguchi method has nothing to do with the presently claimed method.

II. Claim 33 is not anticipated by Sakaguchi et al.

Claim 33 is directed to a method for determining if an animal has been exposed to a specific hemolysin-producing fungus. Sakaguchi already knew that the animal had been exposed to the fungus, as Sakaguchi had administered the fungus to the animal.

Contrary to the Examiner's assertion that the intention or purpose of the invention as set forth in the preamble is not seen as limiting, it is respectfully submitted that the preamble in this case give life to the claimed invention. To read claim 33 as covering all assays detecting fungal hemolysin in a sample would be divorced from reality.

As in *Corning Glass Works v. Sumitomo Electric*, 868 F.2d 1251; 9 USPQ 2d 1962 (Fed. Cir. 1989). The specification makes it clear that the inventors were working on the particular problem of identifying hemolysin-producing fungi and identifying if an animal had been exposed to one of such fungi. As in *Corning, supra*, the preamble gives life and meaning to the claim and provides further positive limitations to the invention so claimed (9 USPQ 2d 1966).

III. Claims 23-29 and 33 Comply with the Written Description Requirement

It is respectfully submitted that the claimed invention is supported by the written description, as there would be no point to the claimed method if the hemolysin produced by the fungus was not unique to that fungus. It is immaterial that the method differentiate among strains or species of fungus. What is claimed is that the method determines if an animal has been exposed to a **specific** hemolysin-producing fungus [emphasis added]. This can only be accomplished if each hemolysin-producing fungus has a hemolysin that is specific for that fungus, so that the fungi can be differentiated from each other. As stated in paragraph 0034, the test is to enable one to identify the source of the hemolysin in a human or other animal that has been exposed to such a fungus. Unless the hemolysin is specific for each

hemolysin-producing fungus, this assay would be worthless other than for a determination that the infection was from a hemolysin-producing fungus.

One skilled in the art reading the present specification and claims would certainly understand that the fungi produce hemolysins that are specific to each fungus producing the hemolysin. It is this specificity that makes it possible to identify a particular fungus that infects a human or other animal. It is respectfully submitted that one skilled in the art would appreciate the requirement for this specificity for the assay to be useful.

IV. Claims 30-32 Comply with the Written Description Requirement

It is clear that paragraphs 0036 and 0037 of the specification as filed teach determining if a building holds fungi that produce hemolysin. The building can be assayed for problematic fungi by taking a sample from the building and assaying it for specific hemolysin-producing fungi. The specification *in toto* explains how one assays for hemolysin-producing fungi. It is respectfully submitted that one skilled in the art could readily appreciate that a building sample can be assayed in the same manner as a sample from an animal.

V. Claims 30-32 Comply with the Enablement Requirement

One skilled in the art, reading the present specification, would readily appreciate that a specific fungus can be detected using antibodies that bind to the fungal hemolysin or active fragments thereof. One skilled in the art of immunoassay is certainly capable of extrapolating methods for detecting samples whether obtained from buildings or animals. It is well known that a specification need not provide the exact wording used in the claims if one skilled in the art can understand what is meant in the disclosure in relation to the claims.

VI. Claims 23-26 Comply with the Written Description Requirement

It is respectfully submitted that one skilled in the art, reading the present specification, would conclude that the fungi being assayed have hemolysins specific to that particular fungus. If the hemolysins were not specific to individual fungi, there would be no point to the present determination, as the only thing determined would be the presence of any hemolysin-producing fungus. It is clear to one skilled in the art that the hemolysin must be specific to a particular fungus for the assay to be useful.

**VII. Claims 30-32 Particularly Point Out and Distinctly Claim
the Subject Matter Which Applicant Regards as the
Invention**


The method of claims 30-32 is for determination if a building contains a hemolysin-producing fungus. One obtains a sample. Then, if hemolysin-producing fungi are present in the building, there is hemolysin in the sample and hemolysin can be obtained from the sample. The remaining steps of the claims infer that there is hemolysin in the sample. It is respectfully submitted that one skilled in the art can readily understand the method claimed herein.

The rejections should be reversed and such is respectfully prayed.

Respectfully submitted,

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